SciLifeLab

Instructions: *Use Times New Roman font size 11, 1.0 pt text space, and* ***maximum three A4 pages****, including any figures.*

Name or type of instrument	**High Content Screening Microscope**
Unit	CBCS
Platform	CBGE
Applicant (Head of Unit)	Anna-Lena Gustavsson
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Instrument, acquisition cost (kSEK)	3500
Funding applied for (kSEK)	3000

Description of the instrument

Describe the instrument, its purpose, and its specific capabilities. If possible, provide a link to a web page describing the type of instrument. Does the instrument represent a new technology at the unit, or is it a replacement/upgrade of current equipment base? Is the instrument unique in terms of service to users nationally?

The current high throughput microscope stationed at CBCS has become outdated and does not meet the needs of the user any longer. With this application we seek funding for a high content screening microscope to replace the current instrument.
Key criteria we are interested in evaluating when purchasing a replacement instrument are:

- Compatibility with multi-well plates, especially spheroid plates
- Time it takes to image one site per well with multiple fluorescence channels
- Number of channels available
- Ability to take confocal images
- Ability to interface with robot arm and plate hotels or CytoMat incubator
- Data storage solutions that are compatible with SciLifeLab infrastructure

Several examples of instruments on the market that would fulfill our requirements are: ImageXpress Confocal HT.ai by Molecular devices, the CellVoyager CQ1 by Yokogawa, the CellInsight CX7 LZR Pro HCS Platform by ThermoFisher Scientific, and the Operetta by PerkinElmer. We have been in contact with several vendors and the price varies depending on configuration of lasers, objectives, temperature control and automation. We will base our decision on image quality and throughput for cheapest price by demoing the instrument (shipping plates to vendor for imaging).

These parameters distinguish the performance of the new machine from the current ImageXpress Micro in the following ways:

1) The current instrument is not confocal.
2) The current time for imaging a single 384-well plate with 4 channels is on the order of 45 minutes per plate. This means that screening the primary set from CBCS (37K small molecules or 106 384-well microtiter plates) is very time consuming and rules out all large-scale live cell assays, as well as some types of hit validation studies.

3) We are not able to effectively run screens on 3D objects such as spheroids or organoids. Imaging 3D objects requires taking multiple planes to cover the depth of the objects. With the current instrument this process takes far too long for any sizeable screen. Additionally, confocal images are really needed for this type of evaluation.
4) The imaging facility at KI (BIC) does not currently have a high content machine set up for screening, so there is no local open access facility. The closest option at BIC is an operetta with similar measurement timeframes as our ImageXpress and no automation.
5) The current instrument does not have a file or experimental storage set up that is compatible with the backup routines at SciLifeLab. We hope to change this to help improve data transfer, backup and analysis in the future.
6) The current microscope has three lasers, while most of the newer machines offer between 5-8 channels.

Statement of need

Describe how the instrument will be crucial for the operations, productivity, development, and competitiveness of your unit. Estimate the need and impact of the instrument from a user perspective. Will the instrument be shared with or used by other units or research groups at SciLifeLab? Also, describe any co-funding plans.

Need at CBCS and Campus Solna

In order to remain competitive in chemical biology on the European and global arena, access to high content imaging is key. This type of instrument can enable both target-based and phenotypic screens using 2D and 3D cell models. A majority of projects coming to CBCS both for large screens and smaller projects are cell-based phenotypic screens or cell-based targeted screens. For these types of projects imaging is an excellent readout choice since each fluorescence channel can report on the localization and quantity of a different protein, organelle or process. At CBCS users have performed screens for compounds modulating protein translocation, localization and co-localization with other proteins. In addition, phenotypic screens examining cellular processes like apoptosis, autophagy, viral infection, protein translation and DNA damage have been conducted using imaging as a read-out.

Open Access users: current and future plans

The current instrument is open access to groups at SciLifeLab and KI area. Once users have received training from CBCS on the instrument and the analysis program, they are able to access the booking calendar. We have had heavy use of the instrument at times, but due to recent technical issues and software challenges this has gone down. Currently this also includes booking of the analysis program and computers as well.

We plan to keep a similar arrangement for the new instrument. A user fee based on instrument cost and personnel time will be applied to all external users once total cost is known. This will provide the Solna SciLifeLab campus with a valuable open-access resource. Depending on the microscope and analysis system purchased, the Kallioniemi team can contribute one additional analysis station for booking outside the one that is currently available at CBCS (ca 100k SEK).

Plans for automation

We plan to integrate the instrument with a robotic arm and plate hotels to increase the throughput and enable efficient use of the system. The arm and plate hotels could be provided by the Fernandez-Capetillo group, when their current microscope is no longer operable (this is a cost of around 200 kSEK)

Plans for co-funding

The Fernandez-Capetillo can contribute an additional 200 kSEK and the Seashore-Ludlow group can contribute 100 kSEK.